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Fanslow, William C.
Lofton, Timothy E.
Sorensen, Eric A.
Youakim, Adel

<120> NECTIN POLYPEPTIDES, POLYNUCLEOTIDES, METHODS OF MAKING AND USE THEREOF

<130> 3101-A <140> Not yet assigned <141> 2001-10-05 <150> 60/238,557 <151> 2000-10-05 <160> 39

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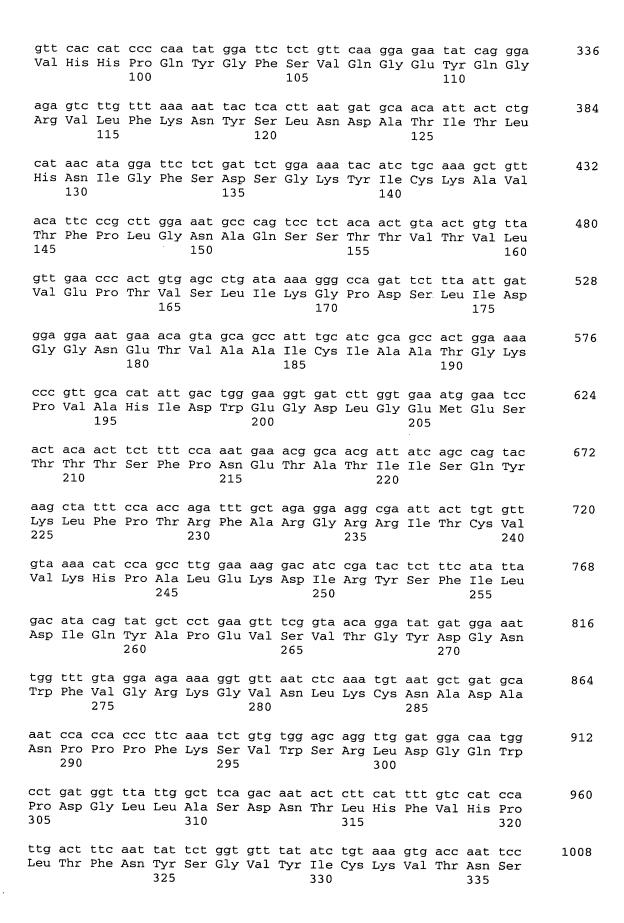
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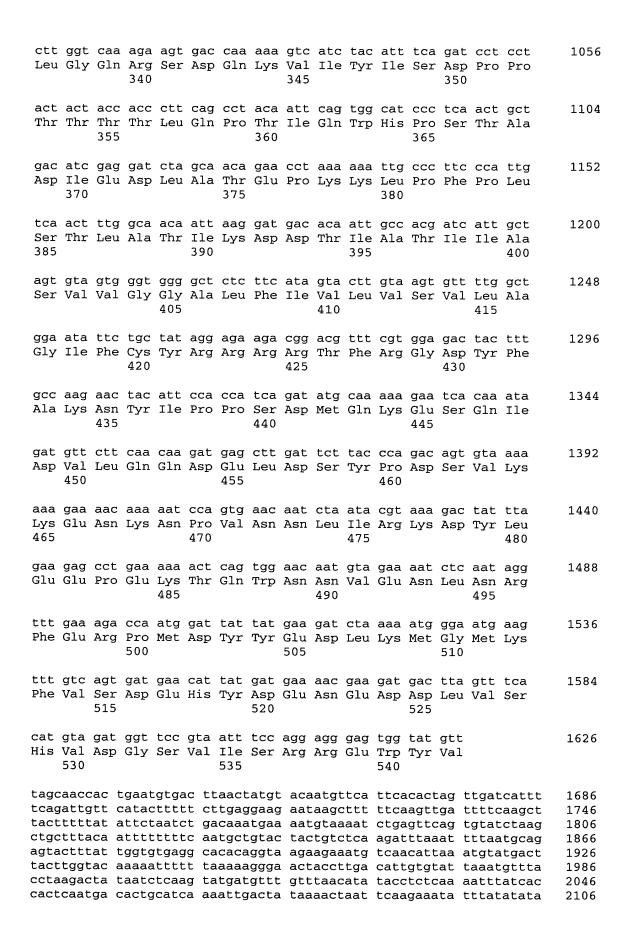
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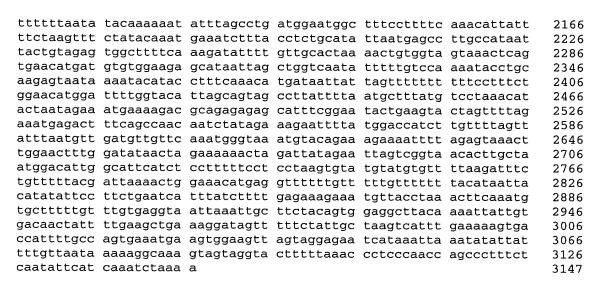
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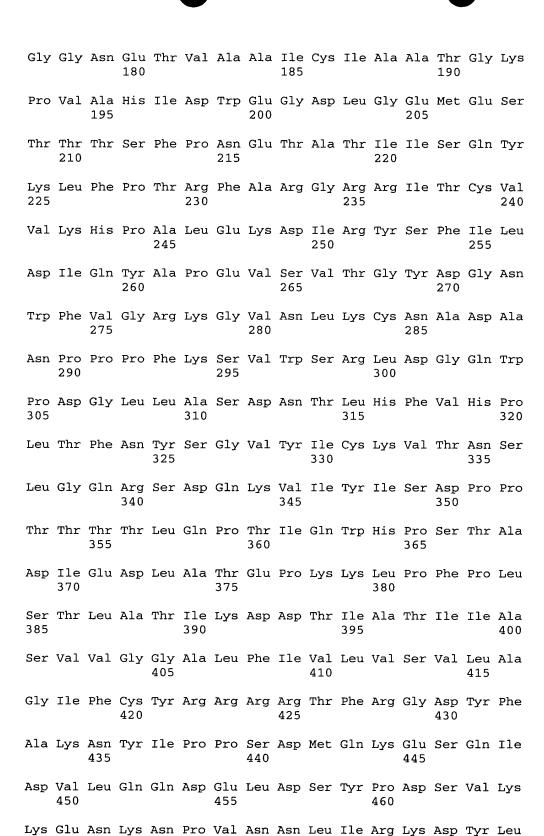
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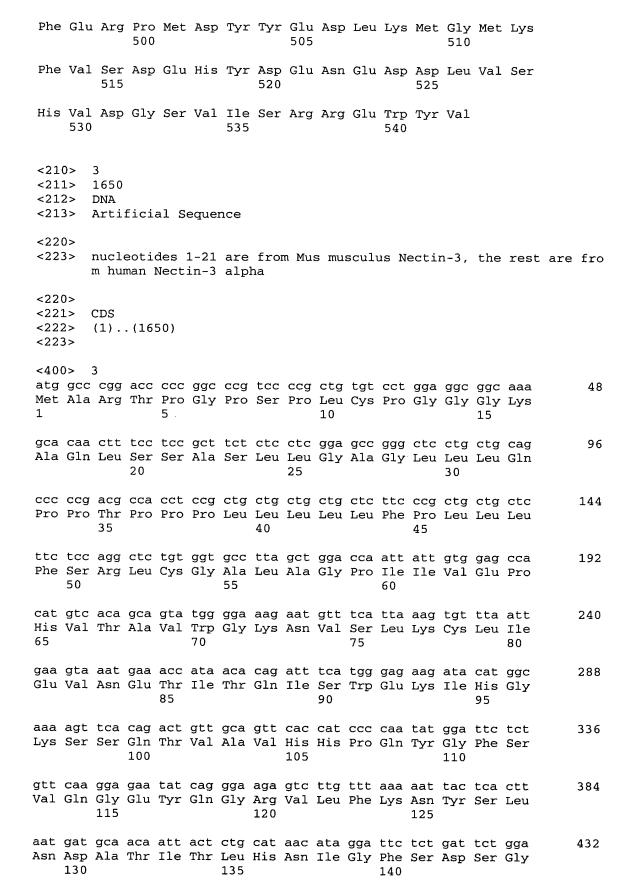
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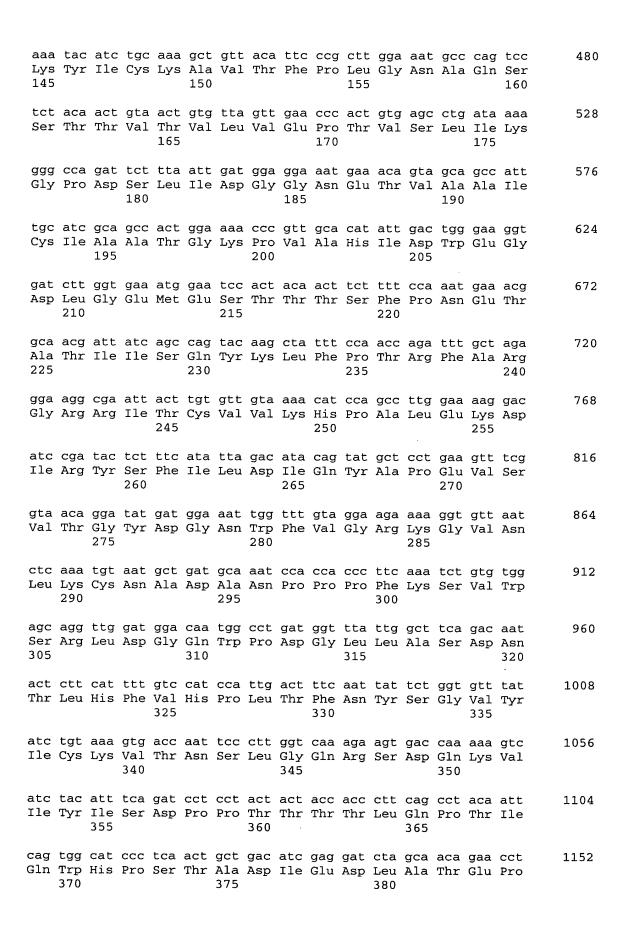
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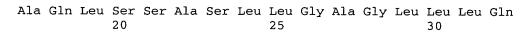
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His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly
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Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Ile 180 185 190

Cys Ile Ala Ala Thr Gly Lys Pro Val Ala His Ile Asp Trp Glu Gly 195 200 205

Asp Leu Gly Glu Met Glu Ser Thr Thr Thr Ser Phe Pro Asn Glu Thr 210 215 220

Ala Thr Ile Ile Ser Gln Tyr Lys Leu Phe Pro Thr Arg Phe Ala Arg 225 230 235 240

Gly Arg Arg Ile Thr Cys Val Val Lys His Pro Ala Leu Glu Lys Asp 245 250 255

Ile Arg Tyr Ser Phe Ile Leu Asp Ile Gln Tyr Ala Pro Glu Val Ser 260 265 270

Val Thr Gly Tyr Asp Gly Asn Trp Phe Val Gly Arg Lys Gly Val Asn 275 280 285

Leu Lys Cys Asn Ala Asp Ala Asn Pro Pro Pro Phe Lys Ser Val Trp 290 295 300

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Ile Tyr Ile Ser Asp Pro Pro Thr Thr Thr Thr Leu Gln Pro Thr Ile 355

Gln Trp His Pro Ser Thr Ala Asp Ile Glu Asp Leu Ala Thr Glu Pro 370

Lys Lys Leu Pro Phe Pro Leu Ser Thr Leu Ala Thr Ile Lys Asp Asp 385 390 395 400

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Thr Phe Arg Gly Asp Tyr Phe Ala Lys Asn Tyr Ile Pro Pro Ser Asp 435 440 445

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Ser Tyr Pro Asp Ser Val Lys Lys Glu Asn Lys Asn Pro Val Asn Asn 465 470 475 480

Leu Ile Arg Lys Asp Tyr Leu Glu Glu Pro Glu Lys Thr Gln Trp Asn 485 490 495

Asn Val Glu Asn Leu Asn Arg Phe Glu Arg Pro Met Asp Tyr Tyr Glu 500 505 510

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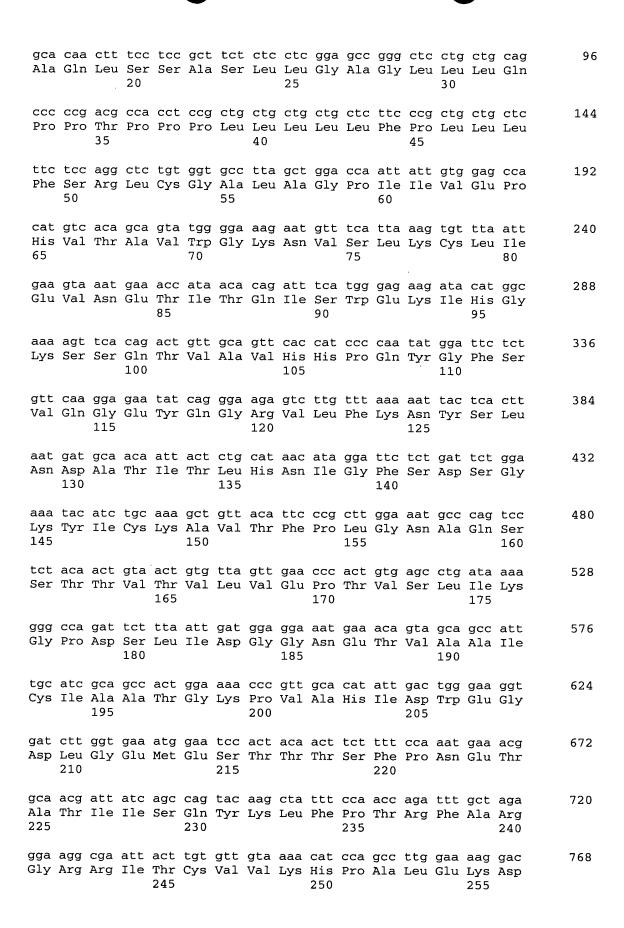
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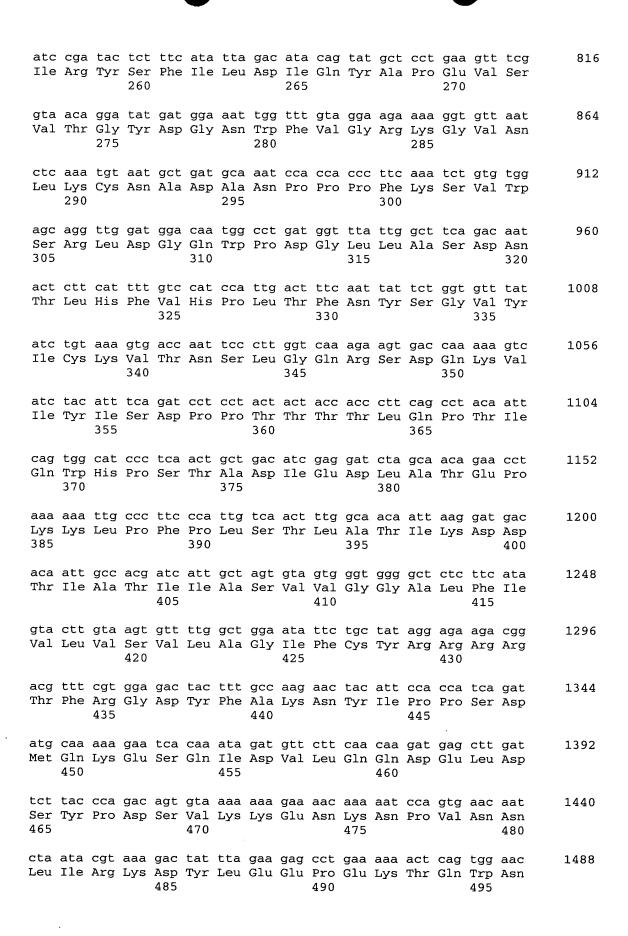
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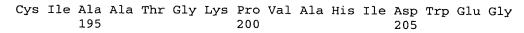
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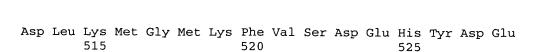


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- Thr Leu His Phe Val His Pro Leu Thr Phe Asn Tyr Ser Gly Val Tyr 325 330 335
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- Lys Lys Leu Pro Phe Pro Leu Ser Thr Leu Ala Thr Ile Lys Asp Asp 385 390 395 400
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- Val Leu Val Ser Val Leu Ala Gly Ile Phe Cys Tyr Arg Arg Arg 420 425 430
- Thr Phe Arg Gly Asp Tyr Phe Ala Lys Asn Tyr Ile Pro Pro Ser Asp 435 440 445
- Met Gln Lys Glu Ser Gln Ile Asp Val Leu Gln Gln Asp Glu Leu Asp 450 455 460
- Ser Tyr Pro Asp Ser Val Lys Lys Glu Asn Lys Asn Pro Val Asn Asn 465 470 475 480
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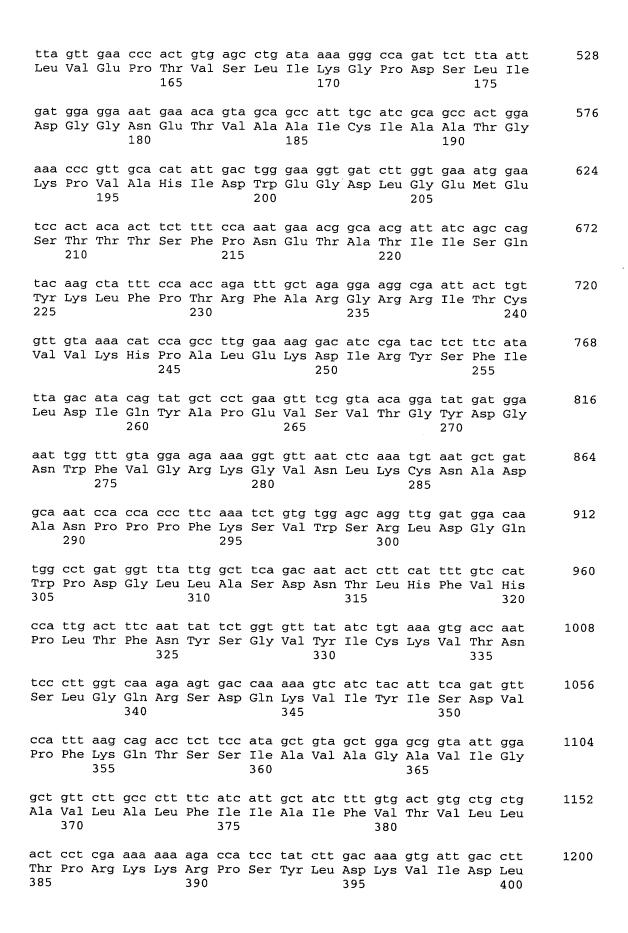
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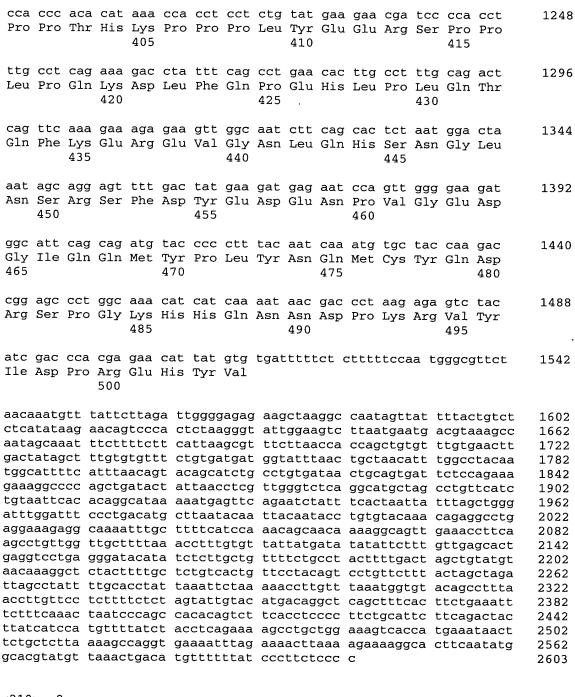
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					ggg Gly												96
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gcc Ala	tta Leu 50	gct Ala	gga Gly	cca Pro	att Ile	att Ile 55	gtg Val	gag Glu	cca Pro	cat His	gtc Val 60	aca Thr	gca Ala	gta Val	tgg Trp	1	192
gga Gly 65	aag Lys	aat Asn	gtt Val	tca Ser	tta Leu 70	aag Lys	tgt Cys	tta Leu	att Ile	gaa Glu 75	gta Val	aat Asn	gaa Glu	acc Thr	ata Ile 80	2	240
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Leu His Asn Ile Gly Phe Ser Asp Ser Gly Lys Tyr Ile Cys Lys Ala 130 135 140

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Lys Pro Val Ala His Ile Asp Trp Glu Gly Asp Leu Gly Glu Met Glu 195 200 205

Ser Thr Thr Thr Ser Phe Pro Asn Glu Thr Ala Thr Ile Ile Ser Gln 210 215 220

Tyr Lys Leu Phe Pro Thr Arg Phe Ala Arg Gly Arg Arg Ile Thr Cys 225 230 235 240

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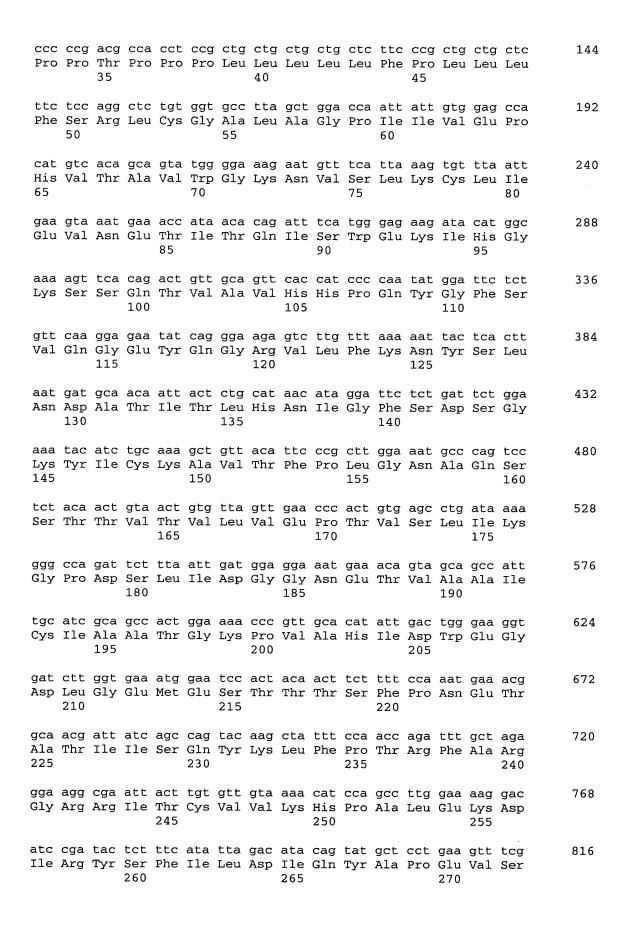
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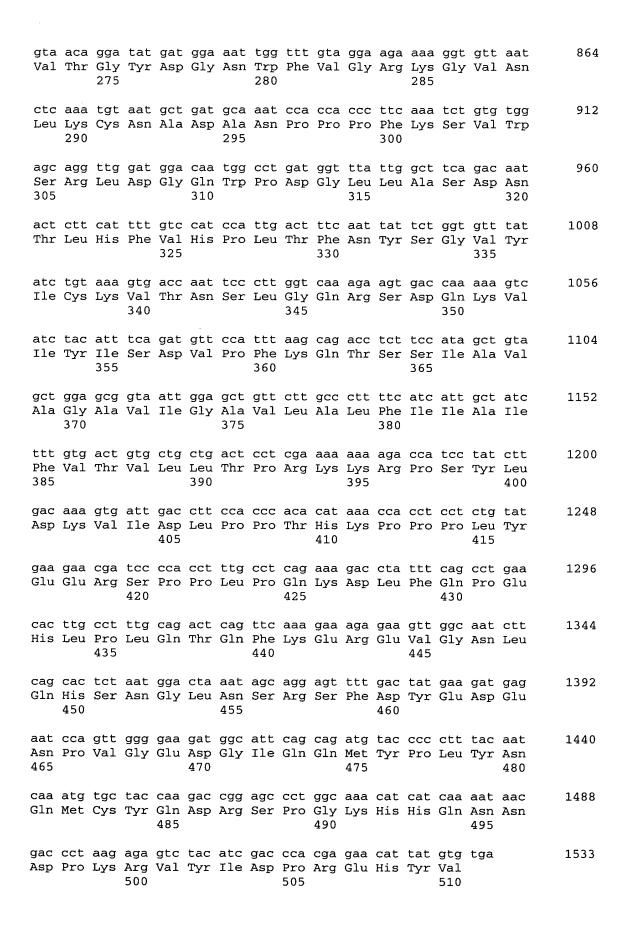
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Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Pro Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly
85 90 95

Lys Ser Ser Gln Thr Val Ala Val His His Pro Gln Tyr Gly Phe Ser 100 105 110

Val Gln Gly Glu Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

Asn Asp Ala Thr Ile Thr Leu His Asn Ile Gly Phe Ser Asp Ser Gly 130 135 140

Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Ile 180 185 190

Cys Ile Ala Ala Thr Gly Lys Pro Val Ala His Ile Asp Trp Glu Gly
195 200 205

Asp Leu Gly Glu Met Glu Ser Thr Thr Thr Ser Phe Pro Asn Glu Thr 210 215 220

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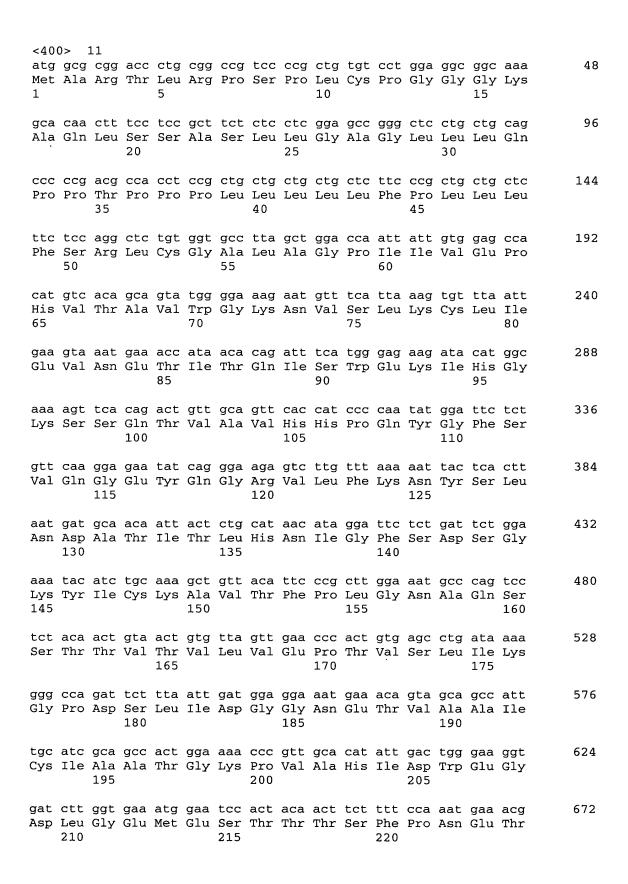
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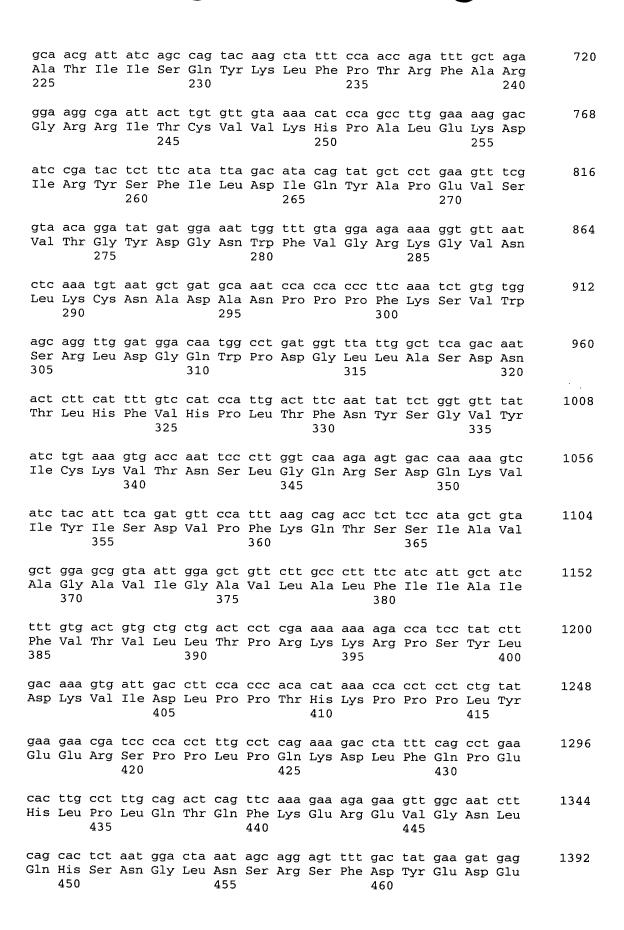
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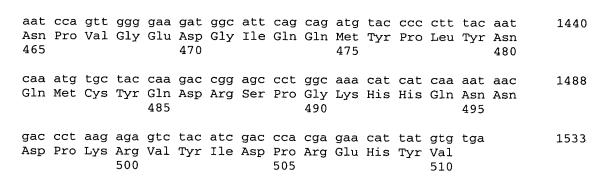
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1 5 10 15

Ala Gln Leu Ser Ser Ala Ser Leu Leu Gly Ala Gly Leu Leu Gln
20 25 30

Pro Pro Thr Pro Pro Pro Leu Leu Leu Leu Leu Phe Pro Leu Leu Leu 35 40 45

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Pro Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly 85 90 95

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Val Gln Gly Glu Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

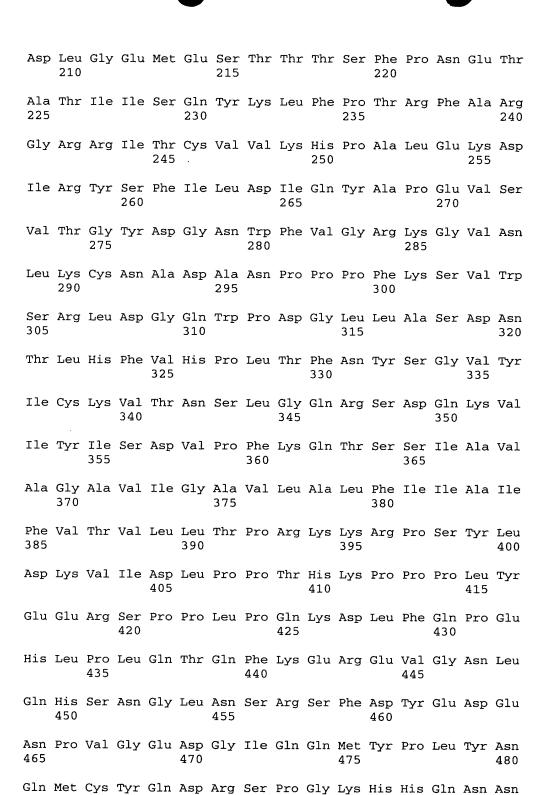
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Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Ile $180 \hspace{1cm} 185 \hspace{1cm} 190$

Cys Ile Ala Ala Thr Gly Lys Pro Val Ala His Ile Asp Trp Glu Gly 195 200 205



Asp Pro Lys Arg Val Tyr Ile Asp Pro Arg Glu His Tyr Val
500 505 510

<210> 13 <211> 634



<213> Artificial Sequence

<220>

<223> fusion protein: human Nectin-3-alpha-Fc

<400> 13

Met Ala Arg Thr Pro Gly Pro Ser Pro Leu Cys Pro Gly Gly Lys
1 5 10 15

Ala Gln Leu Ser Ser Ala Ser Leu Leu Gly Ala Gly Leu Leu Gln 20 25 30

Pro Pro Thr Pro Pro Pro Leu Leu Leu Leu Phe Pro Leu Leu Leu Leu 35 40 45

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Pro Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly 85 90 95

Lys Ser Ser Gln Thr Val Ala Val His His Pro Gln Tyr Gly Phe Ser 100 105 110

Val Gln Gly Glu Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

Asn Asp Ala Thr Ile Thr Leu His Asn Ile Gly Phe Ser Asp Ser Gly 130 135 140

Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Ile 180 185 190

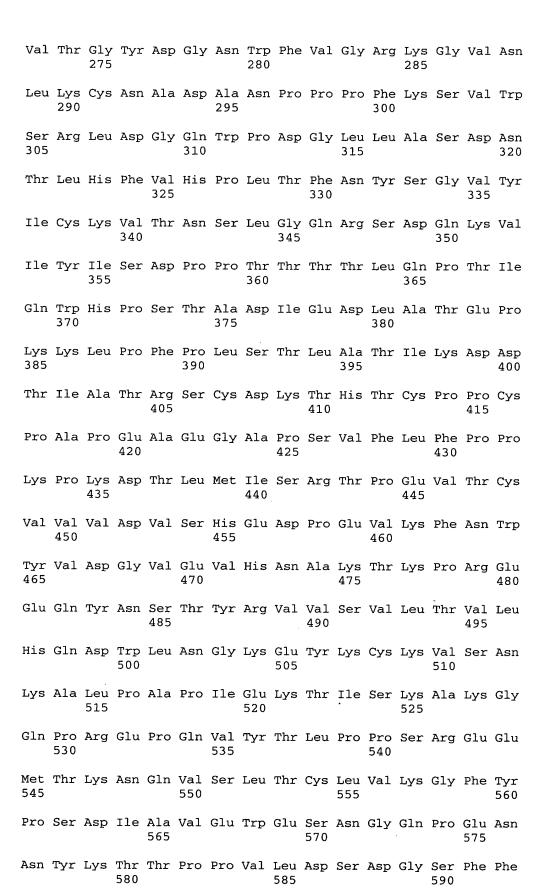
Cys Ile Ala Ala Thr Gly Lys Pro Val Ala His Ile Asp Trp Glu Gly 195 200 205

Asp Leu Gly Glu Met Glu Ser Thr Thr Thr Ser Phe Pro Asn Glu Thr 210 215 220

Ala Thr Ile Ile Ser Gln Tyr Lys Leu Phe Pro Thr Arg Phe Ala Arg 225 230 235 240

Gly Arg Arg Ile Thr Cys Val Val Lys His Pro Ala Leu Glu Lys Asp 245 250 255

Ile Arg Tyr Ser Phe Ile Leu Asp Ile Gln Tyr Ala Pro Glu Val Ser 260 265 270



Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn 595 600

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Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 625 630

<210> 14

<211> 595

<212> PRT

<213> Artificial Sequence

<220>

<223> fusion protein: human Nectin-3-beta-Fc

<400> 14

Met Ala Arg Thr Pro Gly Pro Ser Pro Leu Cys Pro Gly Gly Lys
1 5 10 15

Ala Gln Leu Ser Ser Ala Ser Leu Leu Gly Ala Gly Leu Leu Gln 20 25 30

Pro Pro Thr Pro Pro Pro Leu Leu Leu Leu Phe Pro Leu Leu Leu Leu 35 40

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Pro Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly
85 90 95

Lys Ser Ser Gln Thr Val Ala Val His His Pro Gln Tyr Gly Phe Ser 100 105 110

Val Gln Gly Glu Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

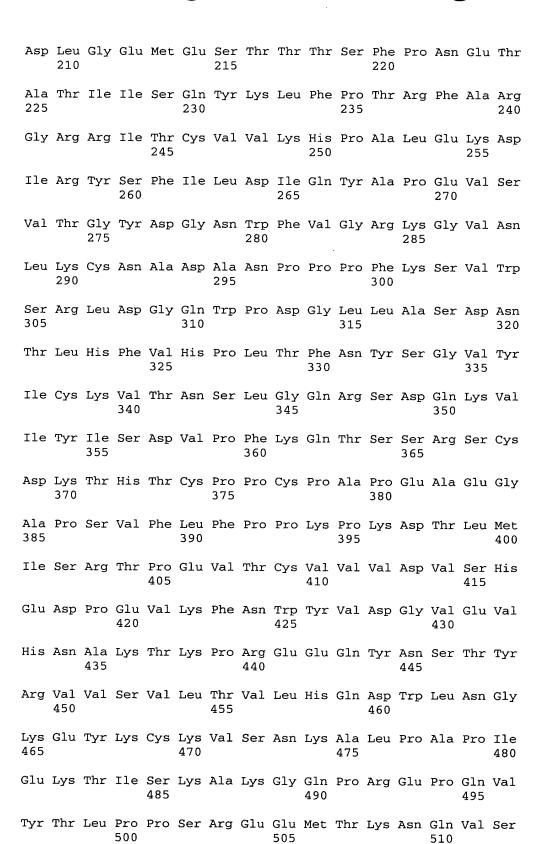
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Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Ile 180 185 190

Cys Ile Ala Ala Thr Gly Lys Pro Val Ala His Ile Asp Trp Glu Gly 195 200 205



Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu

520

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 530 535 540

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 545 550 560

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 565 570 575

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 580 585 590

Pro Gly Lys 595

<210> 15

<211> 426

<212> PRT

<213> Artificial Sequence

<220>

<223> fusion protein: human Nectin-3-alpha-FLAGpolyHis

<400> 15

Met Ala Arg Thr Pro Gly Pro Ser Pro Leu Cys Pro Gly Gly Gly Lys
1 5 10 15

Ala Gln Leu Ser Ser Ala Ser Leu Leu Gly Ala Gly Leu Leu Gln 20 25 30

Pro Pro Thr Pro Pro Pro Leu Leu Leu Leu Leu Phe Pro Leu Leu Leu 35 40 45

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Pro Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly 85 90 95

Lys Ser Ser Gln Thr Val Ala Val His His Pro Gln Tyr Gly Phe Ser 100 105 110

Val Gln Gly Glu Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

Asn Asp Ala Thr Ile Thr Leu His Asn Ile Gly Phe Ser Asp Ser Gly 130 135 140

Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Ile 180 185 190 Cys Ile Ala Ala Thr Gly Lys Pro Val Ala His Ile Asp Trp Glu Gly 195 200 205

Asp Leu Gly Glu Met Glu Ser Thr Thr Thr Ser Phe Pro Asn Glu Thr 210 215 220

Ala Thr Ile Ile Ser Gln Tyr Lys Leu Phe Pro Thr Arg Phe Ala Arg 225 230 235 240

Gly Arg Arg Ile Thr Cys Val Val Lys His Pro Ala Leu Glu Lys Asp 245 250 255

Ile Arg Tyr Ser Phe Ile Leu Asp Ile Gln Tyr Ala Pro Glu Val Ser 260 265 270

Val Thr Gly Tyr Asp Gly Asn Trp Phe Val Gly Arg Lys Gly Val Asn 275 280 285

Leu Lys Cys Asn Ala Asp Ala Asn Pro Pro Pro Phe Lys Ser Val Trp 290 295 300

Ser Arg Leu Asp Gly Gln Trp Pro Asp Gly Leu Leu Ala Ser Asp Asn 305 310 315 320

Thr Leu His Phe Val His Pro Leu Thr Phe Asn Tyr Ser Gly Val Tyr 325 330 335

Ile Cys Lys Val Thr Asn Ser Leu Gly Gln Arg Ser Asp Gln Lys Val 340 345 350

Ile Tyr Ile Ser Asp Pro Pro Thr Thr Thr Leu Gln Pro Thr Ile 355 360 365

Gln Trp His Pro Ser Thr Ala Asp Ile Glu Asp Leu Ala Thr Glu Pro 370 375 380

Lys Lys Leu Pro Phe Pro Leu Ser Thr Leu Ala Thr Ile Lys Asp Asp 385 390 395 400

Thr Ile Ala Thr Arg Ser Gly Ser Ser Asp Tyr Lys Asp Asp Asp Asp 405 410 415

Lys Gly Ser Ser His His His His His 420 425

<210> 16

<211> 387

<212> PRT

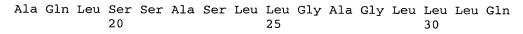
<213> Artificial Sequence

<220>

<223> fusion protein: human Nectin-3-beta-FLAGpolyHis

<400> 16

Met Ala Arg Thr Pro Gly Pro Ser Pro Leu Cys Pro Gly Gly Lys 1 5 10 15



Pro Pro Thr Pro Pro Pro Leu Leu Leu Leu Leu Phe Pro Leu Leu Leu 35 40 45

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Pro Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly
85 90 95

Lys Ser Ser Gln Thr Val Ala Val His His Pro Gln Tyr Gly Phe Ser 100 105 110

Val Gln Gly Glu Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

Asn Asp Ala Thr Ile Thr Leu His Asn Ile Gly Phe Ser Asp Ser Gly 130 135 140

Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Ile 180 185 190

Cys Ile Ala Ala Thr Gly Lys Pro Val Ala His Ile Asp Trp Glu Gly 195 200 205

Asp Leu Gly Glu Met Glu Ser Thr Thr Thr Ser Phe Pro Asn Glu Thr 210 215 220

Ala Thr Ile Ile Ser Gln Tyr Lys Leu Phe Pro Thr Arg Phe Ala Arg 225 230 235 240

Gly Arg Arg Ile Thr Cys Val Val Lys His Pro Ala Leu Glu Lys Asp \$245\$ \$250\$ \$255\$

Ile Arg Tyr Ser Phe Ile Leu Asp Ile Gln Tyr Ala Pro Glu Val Ser 260 265 270

Val Thr Gly Tyr Asp Gly Asn Trp Phe Val Gly Arg Lys Gly Val Asn 275 280 285

Leu Lys Cys Asn Ala Asp Ala Asn Pro Pro Pro Phe Lys Ser Val Trp 290 295 300

Ser Arg Leu Asp Gly Gln Trp Pro Asp Gly Leu Leu Ala Ser Asp Asn 305 310 315 320

Thr Leu His Phe Val His Pro Leu Thr Phe Asn Tyr Ser Gly Val Tyr 325 330 335

Ile Cys Lys Val Thr Asn Ser Leu Gly Gln Arg Ser Asp Gln Lys Val 340 345 . 350

Ile Tyr Ile Ser Asp Val Pro Phe Lys Gln Thr Ser Ser Arg Ser Gly 355 360 365

Ser Ser Asp Tyr Lys Asp Asp Asp Lys Gly Ser Ser His His His 370 375 380

His His His 385

<210> 17

<211> 549

<212> PRT

<213> mus musculus

<400> 17

Met Ala Arg Thr Pro Gly Pro Ala Pro Leu Cys Pro Gly Gly Lys

1 10 15

Ala Gln Leu Ser Ser Ala Phe Pro Pro Ala Ala Gly Leu Leu Pro 20 25 30

Ala Pro Thr Pro Pro Pro Leu Leu Leu Leu Ile Pro Leu Leu Leu 35 40 45

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Ser Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly 85 90 95

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Val Gln Gly Asp Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

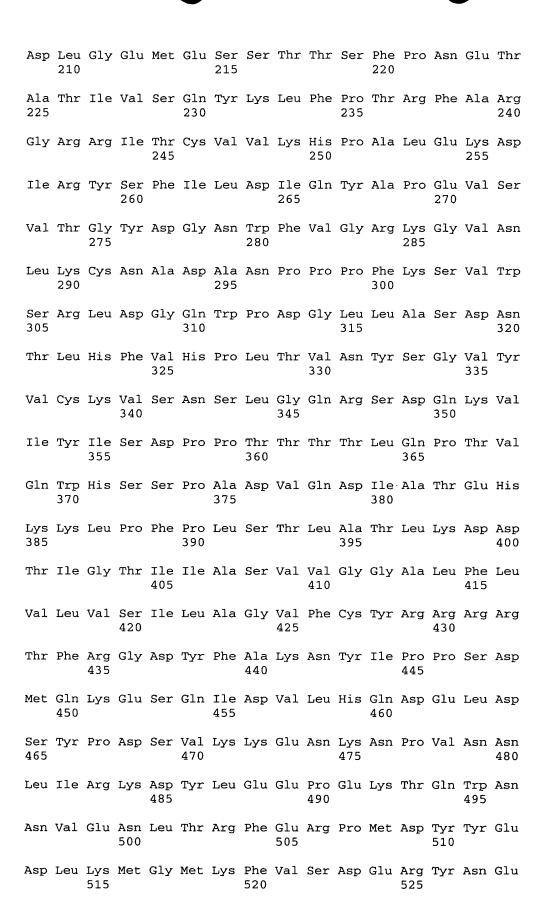
Asn Asp Ala Thr Ile Thr Leu His Asn Ile Gly Phe Ser Asp Ser Gly 130 135 140

Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Val 180 185 . 190

Cys Val Ala Ala Thr Gly Lys Pro Val Ala Gln Ile Asp Trp Glu Gly 195 200 205



Ser Glu Asp Gly Leu Val Ser His Val Asp Gly Ser Val Ile Ser Arg 530 535 540

Arg Glu Trp Tyr Val 545

<210> 18

<211> 510

<212> PRT

<213> mus musculus

<400> 18

Met Ala Arg Thr Pro Gly Pro Ala Pro Leu Cys Pro Gly Gly Gly Lys 1 5 10 15

Ala Gln Leu Ser Ser Ala Phe Pro Pro Ala Ala Gly Leu Leu Pro 20 25 30

Ala Pro Thr Pro Pro Pro Leu Leu Leu Leu Ile Pro Leu Leu Leu 35 40 45

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Ser Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly 85 90 95

Lys Ser Thr Gln Thr Val Ala Val His His Pro Gln Tyr Gly Phe Ser 100 105 110

Val Gln Gly Asp Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

Asn Asp Ala Thr Ile Thr Leu His Asn Ile Gly Phe Ser Asp Ser Gly 130 135 140

Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Val 180 185 190

Cys Val Ala Ala Thr Gly Lys Pro Val Ala Gln Ile Asp Trp Glu Gly
195 200 205

Asp Leu Gly Glu Met Glu Ser Ser Thr Thr Ser Phe Pro Asn Glu Thr 210 215 220

Ala Thr Ile Val Ser Gln Tyr Lys Leu Phe Pro Thr Arg Phe Ala Arg 225 230 235 240

Gly Arg Arg Ile Thr Cys Val Val Lys His Pro Ala Leu Glu Lys Asp 245 250 255

Ile Arg Tyr Ser Phe Ile Leu Asp Ile Gln Tyr Ala Pro Glu Val Ser 260 265 270

Val Thr Gly Tyr Asp Gly Asn Trp Phe Val Gly Arg Lys Gly Val Asn 275 280 285

Leu Lys Cys Asn Ala Asp Ala Asn Pro Pro Pro Phe Lys Ser Val Trp 290 295 300

Ser Arg Leu Asp Gly Gln Trp Pro Asp Gly Leu Leu Ala Ser Asp Asn 305 310 315 320

Thr Leu His Phe Val His Pro Leu Thr Val Asn Tyr Ser Gly Val Tyr
325 330 335

Val Cys Lys Val Ser Asn Ser Leu Gly Gln Arg Ser Asp Gln Lys Val 340 345 350

Ile Tyr Ile Ser Asp Ile Pro Leu Thr Gln Thr Ser Ser Ile Ala Val 355 360 365

Ala Gly Ala Val Ile Gly Ala Val Leu Ala Leu Phe Ile Ile Thr Val 370 375 380

Phe Val Thr Val Leu Leu Thr Pro Arg Lys Lys Arg Pro Ser Tyr Leu 385 390 395 400

Asp Lys Val Ile Asp Leu Pro Pro Thr His Lys Pro Pro Pro Val Tyr 405 410 415

Glu Glu Arg Ile Pro Ser Leu Pro Gln Lys Asp Leu Leu Gly Gln Thr 420 425 430

Glu His Leu Pro Leu Gln Thr Gln Phe Lys Glu Lys Gly Ala Gly Gly 435 440 445

Leu Gln Pro Ser Asn Gly Pro Ile Ser Arg Arg Phe Asp Tyr Glu Asp 450 455 460

Glu Ser Thr Met Gln Glu Asp Gly Thr Gln Arg Met Cys Pro Leu Tyr 465 470 475 480

Ser Gln Met Cys His Gln Asp Arg Ser Pro Arg Gln His His Pro Arg 485 490 495

Asn Pro Glu Arg Leu Tyr Ile Asn Pro Arg Glu His Tyr Val 500 505 510

<210> 19

<211> 438

<212> PRT

<213> mus musculus

<400> 19

Met Ala Arg Thr Pro Gly Pro Ala Pro Leu Cys Pro Gly Gly Lys
1 5 10 15

Ala Gln Leu Ser Ser Ala Phe Pro Pro Ala Ala Gly Leu Leu Pro 20 25 30

Ala Pro Thr Pro Pro Pro Leu Leu Leu Leu Ile Pro Leu Leu Leu 35 40

Phe Ser Arg Leu Cys Gly Ala Leu Ala Gly Ser Ile Ile Val Glu Pro 50 55 60

His Val Thr Ala Val Trp Gly Lys Asn Val Ser Leu Lys Cys Leu Ile 65 70 75 80

Glu Val Asn Glu Thr Ile Thr Gln Ile Ser Trp Glu Lys Ile His Gly 85 90 95

Lys Ser Thr Gln Thr Val Ala Val His His Pro Gln Tyr Gly Phe Ser 100 105 110

Val Gln Gly Asp Tyr Gln Gly Arg Val Leu Phe Lys Asn Tyr Ser Leu 115 120 125

Asn Asp Ala Thr Ile Thr Leu His Asn Ile Gly Phe Ser Asp Ser Gly 130 135 140

Lys Tyr Ile Cys Lys Ala Val Thr Phe Pro Leu Gly Asn Ala Gln Ser 145 150 155 160

Ser Thr Thr Val Thr Val Leu Val Glu Pro Thr Val Ser Leu Ile Lys 165 170 175

Gly Pro Asp Ser Leu Ile Asp Gly Gly Asn Glu Thr Val Ala Ala Val 180 185 190

Cys Val Ala Ala Thr Gly Lys Pro Val Ala Gln Ile Asp Trp Glu Gly 195 200 205

Asp Leu Gly Glu Met Glu Ser Ser Thr Thr Ser Phe Pro Asn Glu Thr 210 215 220

Ala Thr Ile Val Ser Gln Tyr Lys Leu Phe Pro Thr Arg Phe Ala Arg 225 230 235 240

Gly Arg Arg Ile Thr Cys Val Val Lys His Pro Ala Leu Glu Lys Asp 245 250 255

Ile Arg Tyr Ser Phe Ile Leu Asp Ile Gln Tyr Ala Pro Glu Val Ser 260 265 270

Val Thr Gly Tyr Asp Gly Asn Trp Phe Val Gly Arg Lys Gly Val Asn 275 280 285

Leu Lys Cys Asn Ala Asp Ala Asn Pro Pro Pro Phe Lys Ser Val Trp 290 295 300

Ser Arg Leu Asp Gly Gln Trp Pro Asp Gly Leu Leu Ala Ser Asp Asn 305 310 315 320

Thr Leu His Phe Val His Pro Leu Thr Val Asn Tyr Ser Gly Val Tyr 325 330 335

Val Cys Lys Val Ser Asn Ser Leu Gly Gln Arg Ser Asp Gln Lys Val 340 345 350

Ile Tyr Ile Ser Asp Ile Pro Leu Thr Gln Thr Ser Ser Ile Ala Val 355 360 365

Ala Gly Ala Val Ile Gly Ala Val Leu Ala Leu Phe Ile Ile Thr Val 370 375 380

Phe Val Thr Val Leu Leu Thr Pro Arg Lys Lys Arg Pro Ser Tyr Leu 385 390 395 400

Asp Lys Val Ile Asp Leu Pro Pro Thr His Lys Pro Pro Pro Val Tyr 405 410 415

Glu Glu Arg Ile Pro Ser Leu Pro Gln Lys Asp Leu Leu Gly Gln Val 420 425 430

Arg Ala Leu Glu Asp Thr 435

<210> 20

<211> 517

<212> PRT

<213> homo sapiens

<400> 20

Met Ala Arg Met Gly Leu Ala Gly Ala Ala Gly Arg Trp Trp Gly Leu 1 5 10 15

Ala Leu Gly Leu Thr Ala Phe Phe Leu Pro Gly Val His Ser Gln Val 20 25 30

Val Gln Val Asn Asp Ser Met Tyr Gly Phe Ile Gly Thr Asp Val Val
35 40 45

Leu His Cys Ser Phe Ala Asn Pro Leu Pro Ser Val Lys Ile Thr Gln 50 55 60

Val Thr Trp Gln Lys Ser Thr Asn Gly Ser Lys Gln Asn Val Ala Ile 65 70 75 80

Tyr Asn Pro Ser Met Gly Val Ser Val Leu Ala Pro Tyr Arg Glu Arg 85 90 95

Val Glu Phe Leu Arg Pro Ser Phe Thr Asp Gly Thr Ile Arg Leu Ser 100 105 110

Arg Leu Glu Leu Glu Asp Glu Gly Val Tyr Ile Cys Glu Phe Ala Thr 115 120 125

Phe Pro Thr Gly Asn Arg Glu Ser Gln Leu Asn Leu Thr Val Met Ala 130 135 140 Lys Pro Thr Asn Trp Ile Glu Gly Thr Gln Ala Val Leu Arg Ala Lys
145 150 155 160

Lys Gly Gln Asp Asp Lys Val Leu Val Ala Thr Cys Thr Ser Ala Asn 165 170 175

Gly Lys Pro Pro Ser Val Val Ser Trp Glu Thr Arg Leu Lys Gly Glu 180 185 190

Ala Glu Tyr Gln Glu Ile Arg Asn Pro Asn Gly Thr Val Thr Val Ile 195 200 205

Ser Arg Tyr Arg Leu Val Pro Ser Arg Glu Ala His Gln Gln Ser Leu 210 215 220

Ala Cys Ile Val Asn Tyr His Met Asp Arg Phe Lys Glu Ser Leu Thr 225 230 235 240

Leu Asn Val Gln Tyr Glu Pro Glu Val Thr Ile Glu Gly Phe Asp Gly 245 250 255

Asn Trp Tyr Leu Gln Arg Met Asp Val Lys Leu Thr Cys Lys Ala Asp 260 265 270

Ala Asn Pro Pro Ala Thr Glu Tyr His Trp Thr Thr Leu Asn Gly Ser 275 280 285

Leu Pro Lys Gly Val Glu Ala Gln Asn Arg Thr Leu Phe Phe Lys Gly 290 295 300

Pro Ile Asn Tyr Ser Leu Ala Gly Thr Tyr Ile Cys Glu Ala Thr Asn 305 310 315 320

Pro Ile Gly Thr Arg Ser Gly Gln Val Glu Val Asn Ile Thr Glu Phe 325 330 335

Pro Tyr Thr Pro Ser Pro Pro Glu His Gly Arg Arg Ala Gly Pro Val 340 345 350

Pro Thr Ala Ile Ile Gly Gly Val Ala Gly Ser Ile Leu Leu Val Leu 355 360 365

Ile Val Val Gly Gly Ile Val Val Ala Leu Arg Arg Arg His Thr 370 375 380

Phe Lys Gly Asp Tyr Ser Thr Lys Lys His Val Tyr Gly Asn Gly Tyr 385 390 395 400

Ser Lys Ala Gly Ile Pro Gln His His Pro Pro Met Ala Gln Asn Leu 405 410 415

Gln Tyr Pro Asp Asp Ser Asp Asp Glu Lys Lys Ala Gly Pro Leu Gly 420 425 430

Gly Ser Ser Tyr Glu Glu Glu Glu Glu Glu Glu Gly Gly Gly 435 440 445

Gly Glu Arg Lys Val Gly Gly Pro His Pro Lys Tyr Asp Glu Asp Ala 450 455 460 Lys Arg Pro Tyr Phe Thr Val Asp Glu Ala Glu Ala Arg Gln Asp Gly 465 470 475 480

Tyr Gly Asp Arg Thr Leu Gly Tyr Gln Tyr Asp Pro Glu Gln Leu Asp 485 490 495

Leu Ala Glu Asn Met Val Ser Gln Asn Asp Gly Ser Phe Ile Ser Lys 500 505 510

Lys Glu Trp Tyr Val 515

<210> 21

<211> 458

<212> PRT

<213> homo sapiens

<400> 21

Met Ala Arg Met Gly Leu Ala Gly Ala Ala Gly Arg Trp Trp Gly Leu 1 5 10 15

Ala Leu Gly Leu Thr Ala Phe Phe Leu Pro Gly Val His Ser Gln Val 20 25 30

Val Gln Val Asn Asp Ser Met Tyr Gly Phe Ile Gly Thr Asp Val Val 35 40 45

Leu His Cys Ser Phe Ala Asn Pro Leu Pro Ser Val Lys Ile Thr Gln 50 55 60

Val Thr Trp Gln Lys Ser Thr Asn Gly Ser Lys Gln Asn Val Ala Ile 65 . 70 . 75 . 80

Tyr Asn Pro Ser Met Gly Val Ser Val Leu Ala Pro Tyr Arg Glu Arg 85 90 95

Val Glu Phe Leu Arg Pro Ser Phe Thr Asp Gly Thr Ile Arg Leu Ser 100 105 110

Arg Leu Glu Leu Glu Asp Glu Gly Val Tyr Ile Cys Glu Phe Ala Thr 115 120 125

Phe Pro Thr Gly Asn Arg Glu Ser Gln Leu Asn Leu Thr Val Met Ala 130 135 140

Lys Pro Thr Asn Trp Ile Glu Gly Thr Gln Ala Val Leu Arg Ala Lys
145 150 155 160

Lys Gly Gln Asp Asp Lys Val Leu Val Ala Thr Cys Thr Ser Ala Asn 165 170 175

Gly Lys Pro Pro Ser Val Val Ser Trp Glu Thr Arg Leu Lys Gly Glu 180 185 190

Ala Glu Tyr Gln Glu Ile Arg Asn Pro Asn Gly Thr Val Thr Val Ile 195 200 205 Ser Arg Tyr Arg Leu Val Pro Ser Arg Glu Ala His Gln Gln Ser Leu 210 215 220

Ala Cys Ile Val Asn Tyr His Met Asp Arg Phe Lys Glu Ser Leu Thr 225 230 235 240

Leu Asn Val Gln Tyr Glu Pro Glu Val Thr Ile Glu Gly Phe Asp Gly 245 250 255

Asn Trp Tyr Leu Gln Arg Met Asp Val Lys Leu Thr Cys Lys Ala Asp 260 265 270

Ala Asn Pro Pro Ala Thr Glu Tyr His Trp Thr Thr Leu Asn Gly Ser 275 280 285

Leu Pro Lys Gly Val Glu Ala Gln Asn Arg Thr Leu Phe Phe Lys Gly 290 295 300

Pro Ile Asn Tyr Ser Leu Ala Gly Thr Tyr Ile Cys Glu Ala Thr Asn 305 310 315 320

Pro Ile Gly Thr Arg Ser Gly Gln Val Glu Val Asn Ile Thr Glu Lys
325 330 335

Pro Arg Pro Gln Arg Gly Leu Gly Ser Ala Ala Arg Leu Leu Ala Gly 340 345

Thr Val Ala Val Phe Leu Ile Leu Val Ala Val Leu Thr Val Phe 355 360 365

Leu Tyr Asn Arg Gln Gln Lys Ser Pro Pro Glu Thr Asp Gly Ala Gly 370 375 380

Thr Asp Gln Pro Leu Ser Gln Lys Pro Glu Pro Ser Pro Ser Arg Gln 385 390 395 400

Ser Ser Leu Val Pro Glu Asp Ile Gln Val Val His Leu Asp Pro Gly 405 410 415

Pro Pro Tyr Tyr Asp Leu Gly Val Ser Pro Ser Tyr His Pro Ser Val 435 440 445

Arg Thr Thr Glu Pro Arg Gly Glu Cys Pro 450 455

<210> 22

<211> 479

<212> PRT

<213> homo sapiens

<400> 22

Met Ala Arg Ala Ala Leu Leu Pro Ser Arg Ser Pro Pro Thr Pro 1 5 10 15

Leu Leu Trp Pro Leu Leu Leu Leu Leu Leu Leu Glu Thr Gly Ala Gln 20 25 30

Asp Val Arg Val Gln Val Leu Pro Glu Val Arg Gly Gln Leu Gly Gly 35 40 45

Thr Val Glu Leu Pro Cys His Leu Leu Pro Pro Val Pro Gly Leu Tyr 50 55 60

Ile Ser Leu Val Thr Trp Gln Arg Pro Asp Ala Pro Ala Asn His Gln 65 70 75 80

Asn Val Ala Ala Phe His Pro Lys Met Gly Pro Ser Phe Pro Ser Pro 85 90 95

Lys Pro Gly Ser Glu Arg Leu Ser Phe Val Ser Ala Lys Gln Ser Thr 100 105 110

Gly Gln Asp Thr Glu Ala Glu Leu Gln Asp Ala Thr Leu Ala Leu His 115 120 125

Gly Leu Thr Val Glu Asp Glu Gly Asn Tyr Thr Cys Glu Phe Ala Thr 130 135 140

Phe Pro Lys Gly Ser Val Arg Gly Met Thr Trp Leu Arg Val Ile Ala 145 150 155 160

Lys Pro Lys Asn Gln Ala Glu Ala Gln Lys Val Thr Phe Ser Gln Asp 165 170 175

Pro Thr Thr Val Ala Leu Cys Ile Ser Lys Glu Gly Arg Pro Pro Ala 180 185 190

Arg Ile Ser Trp Leu Ser Ser Leu Asp Trp Glu Ala Lys Glu Thr Gln
195 200 205

Val Ser Gly Thr Leu Ala Gly Thr Val Thr Val Thr Ser Arg Phe Thr 210 215 220

Leu Val Pro Ser Gly Arg Ala Asp Gly Val Thr Val Thr Cys Lys Val 225 230 235 240

Glu His Glu Ser Phe Glu Glu Pro Ala Leu Ile Pro Val Thr Leu Ser 245 250 255

Val Arg Tyr Pro Pro Glu Val Ser Ile Ser Gly Tyr Asp Asp Asn Trp 260 265 270

Tyr Leu Gly Arg Thr Asp Ala Thr Leu Ser Cys Asp Val Arg Ser Asn 275 280 285

Pro Glu Pro Thr Gly Tyr Asp Trp Ser Thr Thr Ser Gly Thr Phe Pro 290 295 300

Thr Ser Ala Val Ala Gln Gly Ser Gln Leu Val Ile His Ala Val Asp 305 310 315 320

Ser Leu Phe Asn Thr Thr Phe Val Cys Thr Val Thr Asn Ala Val Gly 325 330 335

Met Gly Arg Ala Glu Gln Val Ile Phe Val Arg Glu Thr Pro Arg Ala 340 345 350

Ser Pro Arg Asp Val Gly Pro Leu Val Trp Gly Ala Val Gly Gly Thr 355 360 365

Leu Leu Val Leu Leu Leu Ala Gly Gly Ser Leu Ala Phe Ile Leu 370 375 380

Leu Arg Val Arg Arg Arg Lys Ser Pro Gly Gly Ala Gly Gly 385 390 395 400

Ala Ser Gly Asp Gly Gly Phe Tyr Asp Pro Lys Ala Gln Val Leu Gly
405 410 415

Asn Gly Asp Pro Val Phe Trp Thr Pro Val Val Pro Gly Pro Met Glu 420 425 430

Pro Asp Gly Lys Asp Glu Glu Glu Glu Glu Glu Glu Glu Lys Ala Glu 435 440 445

Lys Gly Leu Met Leu Pro Pro Pro Pro Ala Leu Glu Asp Asp Met Glu 450 455 460

Ser Gln Leu Asp Gly Ser Leu Ile Ser Arg Arg Ala Val Tyr Val 465 470 475

<210> 23

<211> 538

<212> PRT

<213> homo sapiens

<400> 23

Met Ala Arg Ala Ala Leu Leu Pro Ser Arg Ser Pro Pro Thr Pro 1 5 10 15

Leu Leu Trp Pro Leu Leu Leu Leu Leu Leu Glu Thr Gly Ala Gln 20 25 30

Asp Val Arg Val Gln Val Leu Pro Glu Val Arg Gly Gln Leu Gly Gly 35 40 45

Thr Val Glu Leu Pro Cys His Leu Leu Pro Pro Val Pro Gly Leu Tyr 50 55 60

Ile Ser Leu Val Thr Trp Gln Arg Pro Asp Ala Pro Ala Asn His Gln 65 70 75 80

Asn Val Ala Ala Phe His Pro Lys Met Gly Pro Ser Phe Pro Ser Pro 85 90 95

Lys Pro Gly Ser Glu Arg Leu Ser Phe Val Ser Ala Lys Gln Ser Thr 100 105 110

Gly Gln Asp Thr Glu Ala Glu Leu Gln Asp Ala Thr Leu Ala Leu His 115 120 125

Gly Leu Thr Val Glu Asp Glu Gly Asn Tyr Thr Cys Glu Phe Ala Thr 130 135 140

Phe Pro Lys Gly Ser Val Arg Gly Met Thr Trp Leu Arg Val Ile Ala 145 Lys Pro Lys Asn Gln Ala Glu Ala Gln Lys Val Thr Phe Ser Gln Asp Pro Thr Thr Val Ala Leu Cys Ile Ser Lys Glu Gly Arg Pro Pro Ala Arg Ile Ser Trp Leu Ser Ser Leu Asp Trp Glu Ala Lys Glu Thr Gln 200 Val Ser Gly Thr Leu Ala Gly Thr Val Thr Val Thr Ser Arg Phe Thr 210 215 Leu Val Pro Ser Gly Arg Ala Asp Gly Val Thr Val Thr Cys Lys Val Glu His Glu Ser Phe Glu Glu Pro Ala Leu Ile Pro Val Thr Leu Ser Val Arg Tyr Pro Pro Glu Val Ser Ile Ser Gly Tyr Asp Asp Asn Trp Tyr Leu Gly Arg Thr Asp Ala Thr Leu Ser Cys Asp Val Arg Ser Asn 280 Pro Glu Pro Thr Gly Tyr Asp Trp Ser Thr Thr Ser Gly Thr Phe Pro Thr Ser Ala Val Ala Gln Gly Ser Gln Leu Val Ile His Ala Val Asp 310 315 Ser Leu Phe Asn Thr Thr Phe Val Cys Thr Val Thr Asn Ala Val Gly Met Gly Arg Ala Glu Gln Val Ile Phe Val Arg Glu Thr Pro Asn Thr Ala Gly Ala Gly Ala Thr Gly Gly Ile Ile Gly Gly Ile Ile Ala Ala 360 Ile Ile Ala Thr Ala Val Ala Ala Thr Gly Ile Leu Ile Cys Arg Gln 375 Gln Arg Lys Glu Gln Thr Leu Gln Gly Ala Glu Glu Asp Glu Asp Leu 390 395 Glu Gly Pro Pro Ser Tyr Lys Pro Pro Thr Pro Lys Ala Lys Leu Glu 405 410 Ala Gln Glu Met Pro Ser Gln Leu Phe Thr Leu Gly Ala Ser Glu His 425 Ser Pro Leu Lys Thr Pro Tyr Phe Asp Ala Gly Ala Ser Cys Thr Glu 435 Gln Glu Met Pro Arg Tyr His Glu Leu Pro Thr Leu Glu Glu Arg Ser 455

Gly Pro Leu His Pro Gly Ala Thr Ser Leu Gly Ser Pro Ile Pro Val 465 470 475 480

Pro Pro Gly Pro Pro Ala Val Glu Asp Val Ser Leu Asp Leu Glu Asp 485 490 495

Glu Glu Glu Glu Glu Glu Glu Tyr Leu Asp Lys Ile Asn Pro Ile
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Tyr Asp Ala Leu Ser Tyr Ser Ser Pro Ser Asp Ser Tyr Gln Gly Lys 515 520 525

Gly Phe Val Met Ser Arg Ala Met Tyr Val 530 535

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<213> homo sapiens

<400> 24

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Glu Leu Glu Thr Ser Asp Val Val Thr Val Val Leu Gly Gln Asp Ala 35 40 45

Lys Leu Pro Cys Phe Tyr Arg Gly Asp Ser Gly Glu Gln Val Gly Gln 50 60

Val Ala Trp Ala Arg Val Asp Ala Gly Glu Gly Ala Gln Glu Leu Ala 65 70 75 80

Leu Leu His Ser Lys Tyr Gly Leu His Val Ser Pro Ala Tyr Glu Gly
85 90 95

Arg Val Glu Gln Pro Pro Pro Pro Arg Asn Pro Leu Asp Gly Ser Val 100 105 110

Leu Leu Arg Asn Ala Val Gln Ala Asp Glu Gly Glu Tyr Glu Cys Arg 115 120 125

Val Ser Thr Phe Pro Ala Gly Ser Phe Gln Ala Arg Leu Arg Leu Arg 130 135 140

Val Met Val Pro Pro Leu Pro Ser Leu Asn Pro Gly Pro Ala Leu Glu 145 150 155 160

Glu Gly Gln Gly Leu Thr Leu Ala Ala Ser Cys Thr Ala Glu Gly Ser 165 170 175

Pro Ala Pro Ser Val Thr Trp Asp Thr Glu Val Lys Gly Thr Thr Ser 180 185 190

Ser Arg Ser Phe Lys His Ser Arg Ser Ala Ala Val Thr Ser Glu Phe 195 200 205

His Leu Val Pro Ser Arg Ser Met Asn Gly Gln Pro Leu Thr Cys Val Val Ser His Pro Gly Leu Leu Gln Asp Gln Arg Ile Thr His Ile Leu His Val Ser Phe Leu Ala Glu Ala Ser Val Arg Gly Leu Glu Asp Gln 250 Asn Leu Trp His Ile Gly Arg Glu Gly Ala Met Leu Lys Cys Leu Ser Glu Gly Gln Pro Pro Pro Ser Tyr Asn Trp Thr Arg Leu Asp Gly Pro Leu Pro Ser Gly Val Arg Val Asp Gly Asp Thr Leu Gly Phe Pro Pro Leu Thr Thr Glu His Ser Gly Ile Tyr Val Cys His Val Ser Asn Glu Phe Ser Ser Arg Asp Ser Gln Val Thr Val Asp Val Leu Asp Pro Gln 330 Glu Asp Ser Gly Lys Gln Val Asp Leu Val Ser Ala Ser Val Val Val Val Gly Val Ile Ala Ala Leu Leu Phe Cys Leu Leu Val Val Val Val Val Leu Met Ser Arg Tyr His Arg Arg Lys Ala Gln Gln Met Thr Gln 375 Lys Tyr Glu Glu Leu Thr Leu Thr Arg Glu Asn Ser Ile Arg Arg 390 395 Leu His Ser His His Thr Asp Pro Arg Ser Gln Pro Glu Glu Ser Val 410 Gly Leu Arg Ala Glu Gly His Pro Asp Ser Leu Lys Asp Asn Ser Ser Cys Ser Val Met Ser Glu Glu Pro Glu Gly Arg Ser Tyr Ser Thr Leu 440 Thr Thr Val Arg Glu Ile Glu Thr Gln Thr Glu Leu Leu Ser Pro Gly 450 Ser Gly Arg Ala Glu Glu Glu Glu Asp Gln Asp Glu Gly Ile Lys Gln 470 Ala Met Asn His Phe Val Gln Glu Asn Gly Thr Leu Arg Ala Lys Pro Thr Gly Asn Gly Ile Tyr Ile Asn Gly Arg Gly His Leu Val 505



<213> homo sapiens

<400> 25

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Ala Pro Thr Gln Val Pro Gly Phe Leu Gly Asp Ser Val Thr Leu Pro 35 40 45

Cys Tyr Leu Gln Val Pro Asn Met Glu Val Thr His Val Ser Gln Leu 50 55 60

Thr Trp Ala Arg His Gly Glu Ser Gly Ser Met Ala Val Phe His Gln 65 70 75 80

Thr Gln Gly Pro Ser Tyr Ser Glu Ser Lys Arg Leu Glu Phe Val Ala 85 90 95

Ala Arg Leu Gly Ala Glu Leu Arg Asn Ala Ser Leu Arg Met Phe Gly 100 105 110

Leu Arg Val Glu Asp Glu Gly Asn Tyr Thr Cys Leu Phe Val Thr Phe 115 120 125

Pro Gln Gly Ser Arg Ser Val Asp Ile Trp Leu Arg Val Leu Ala Lys 130 135 140

Pro Gln Asn Thr Ala Glu Val Gln Lys Val Gln Leu Thr Gly Glu Pro 145 150 155 160

Val Pro Met Ala Arg Cys Val Ser Thr Gly Gly Arg Pro Pro Ala Gln
165 170 175

Ile Thr Trp His Ser Asp Leu Gly Gly Met Pro Asn Thr Ser Gln Val

Pro Gly Phe Leu Ser Gly Thr Val Thr Val Thr Ser Leu Trp Ile Leu 195 200 205

Val Pro Ser Ser Gln Val Asp Gly Lys Asn Val Thr Cys Lys Val Glu 210 215 220

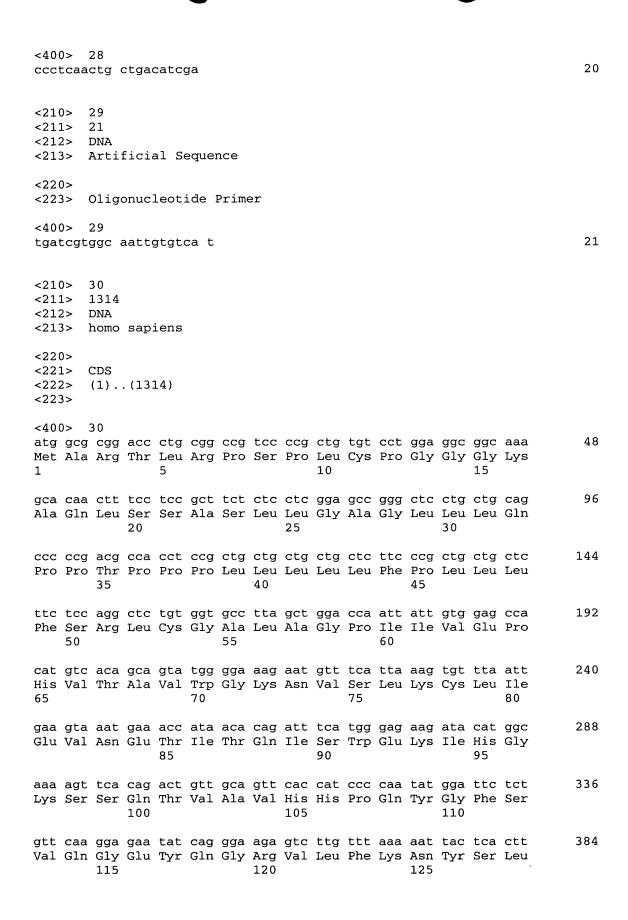
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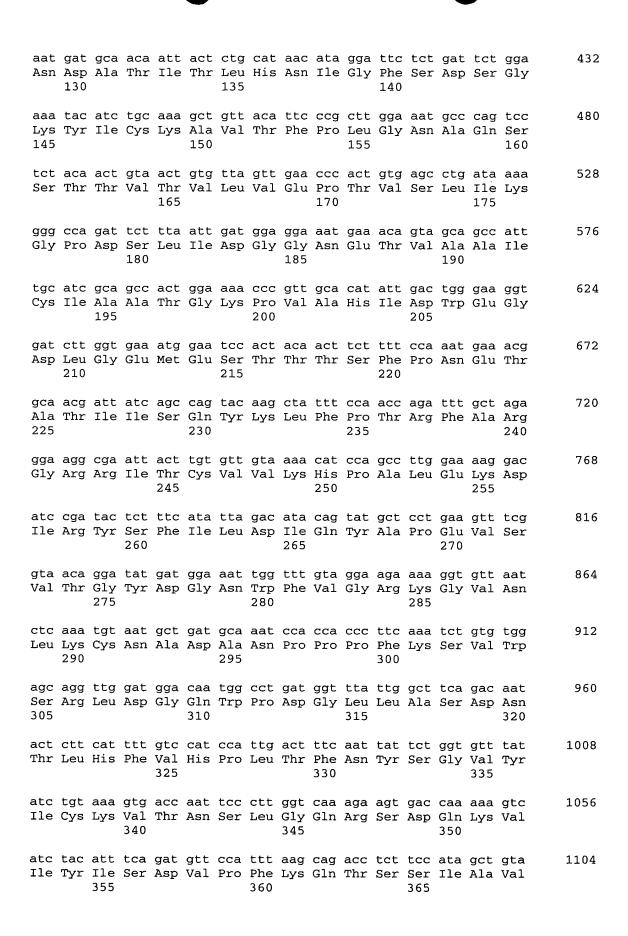
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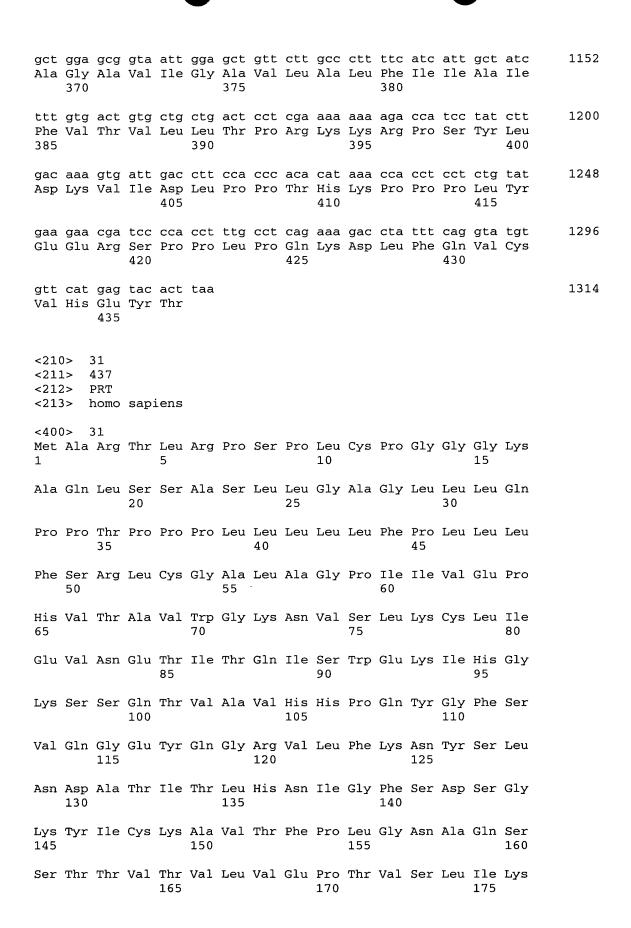
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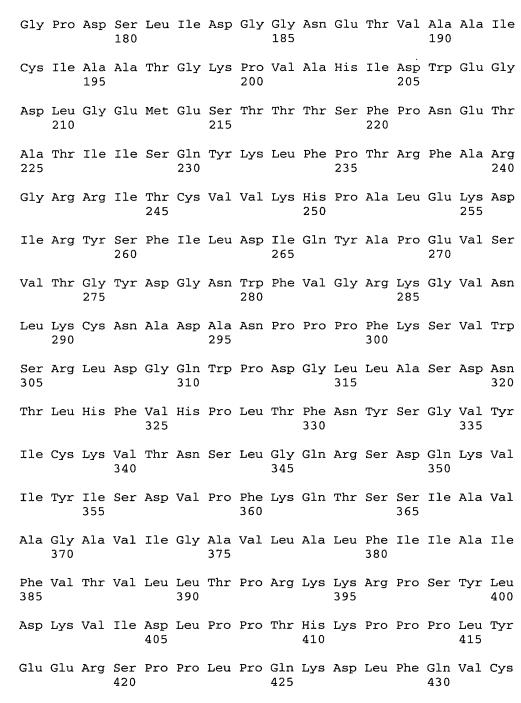
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Pro Il 305	e Asn	Thr	Thr	Leu 310	Ile	Суѕ	Asn	Val	Thr 315	Asn	Ala	Leu	Gly	Ala 320		
Arg Gl	n Ala	Glu	Leu 325	Thr	Val	Gln	Val	Lys 330	Glu	Gly	Pro	Pro	Ser 335	Glu		
His Se	r Gly	Ile 340	Ser	Arg	Asn	Ala	Ile 345	Ile	Phe	Leu	Val	Leu 350	Gly	Ile		
Leu Va	l Phe 355	Leu	Ile	Leu	Leu	Gly 360	Ile	Gly	Ile	Tyr	Phe 365	Tyr	Trp	Ser		
Lys Cy 37		Arg	Glu	Val	Leu 375	Trp	His	Cys	His	Leu 380	Cys	Pro	Ser	Ser		
Thr Gl 385	u His	Ala	Ser	Ala 390	Ser	Ala	Asn	Gly	His 395	Val	Ser	Tyr	Ser	Ala 400		
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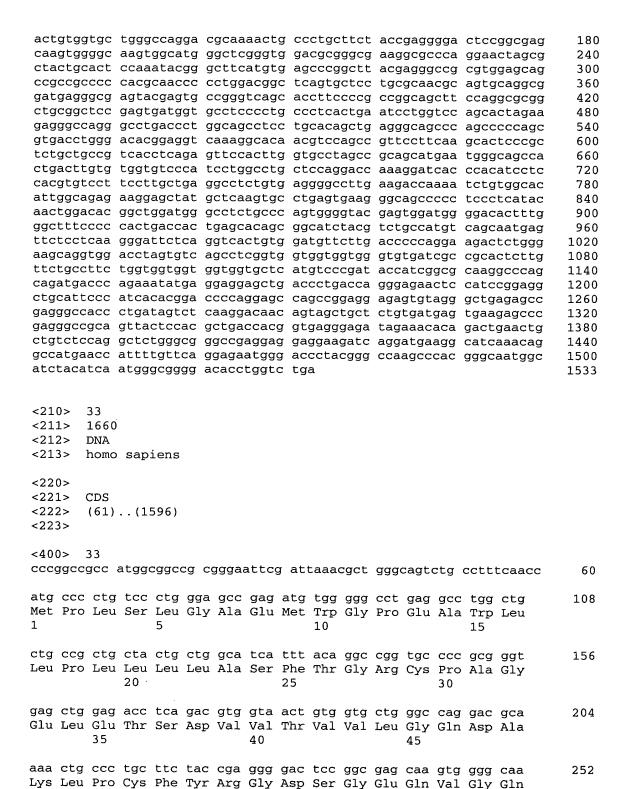
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50

65



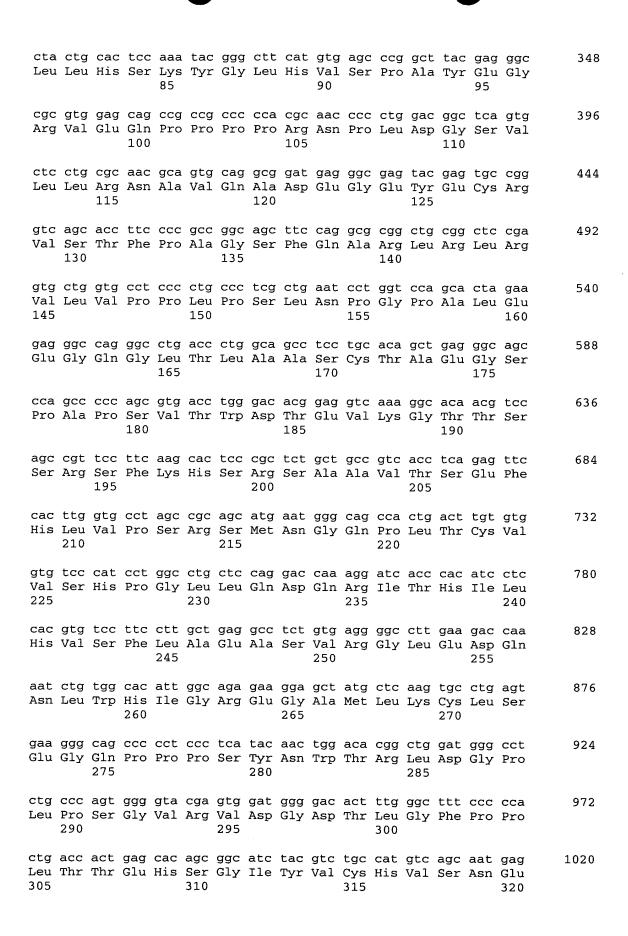


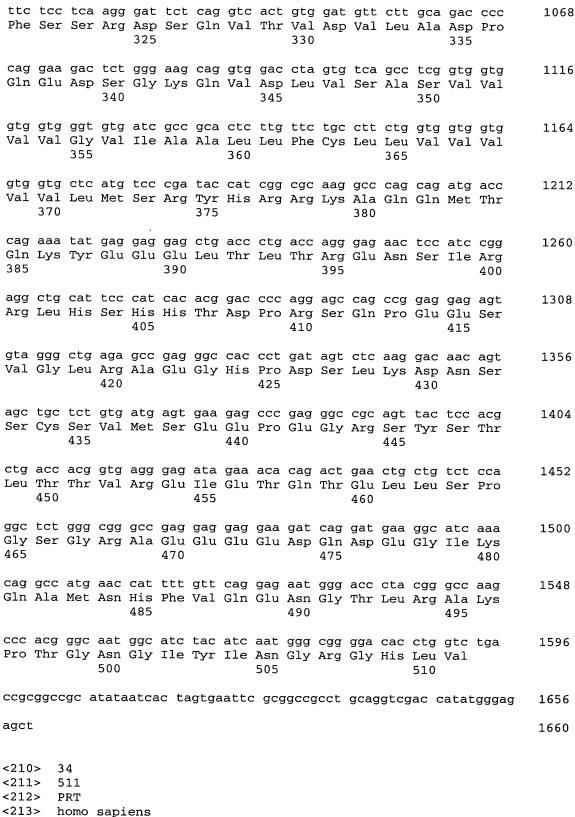
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His Leu Val Pro Ser Arg Ser Met Asn Gly Gln Pro Leu Thr Cys Val 210

Val Ser His Pro Gly Leu Leu Gln Asp Gln Arg Ile Thr His Ile Leu 225

235

Val Ser His Pro Gly Leu Leu Gln Asp Gln Arg 235

Ser Arg Ser Phe Lys His Ser Arg Ser Ala Ala Val Thr Ser Glu Phe 195 200 205

His Val Ser Phe Leu Ala Glu Ala Ser Val Arg Gly Leu Glu Asp Gln 245 250 255

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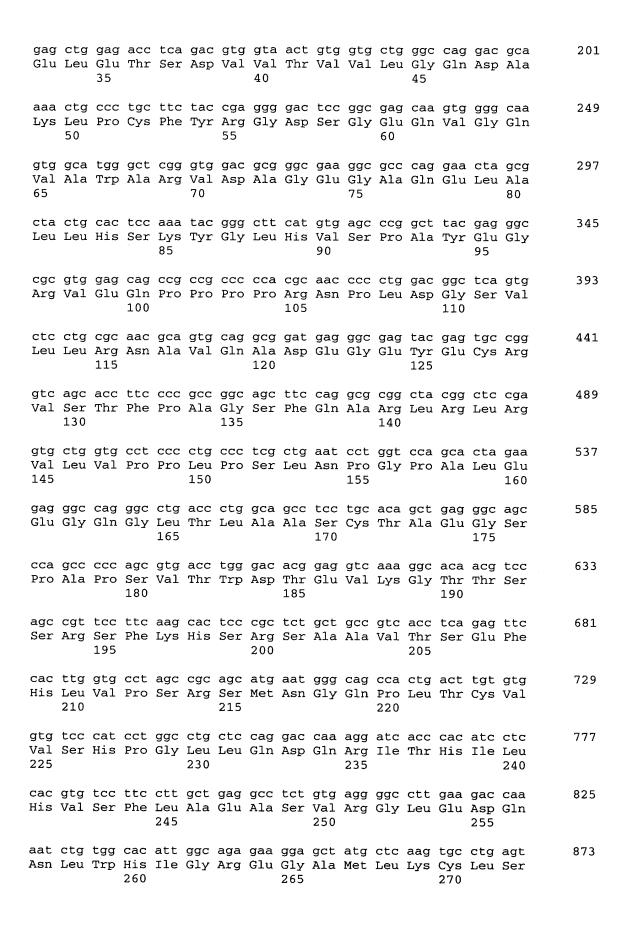
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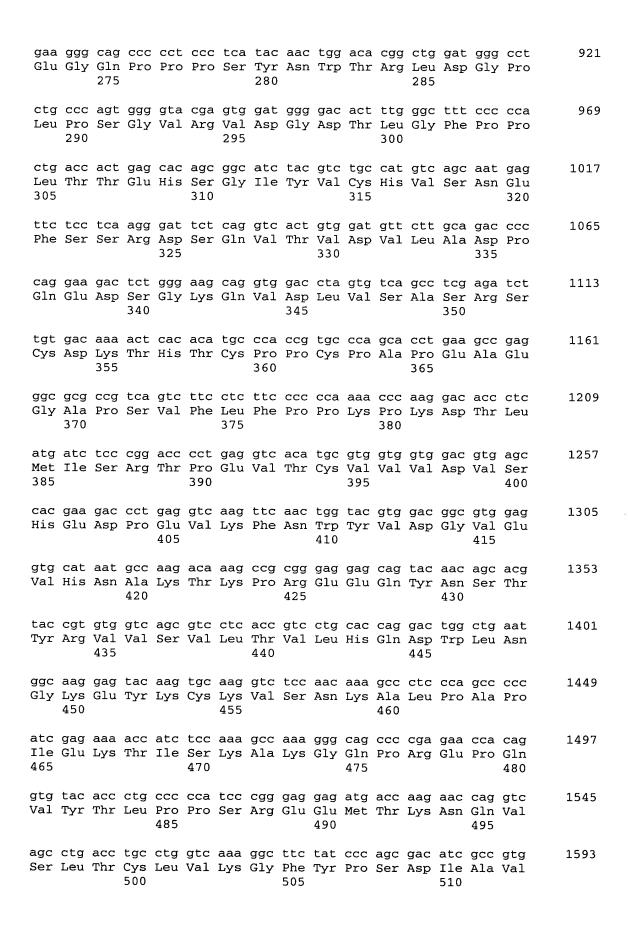
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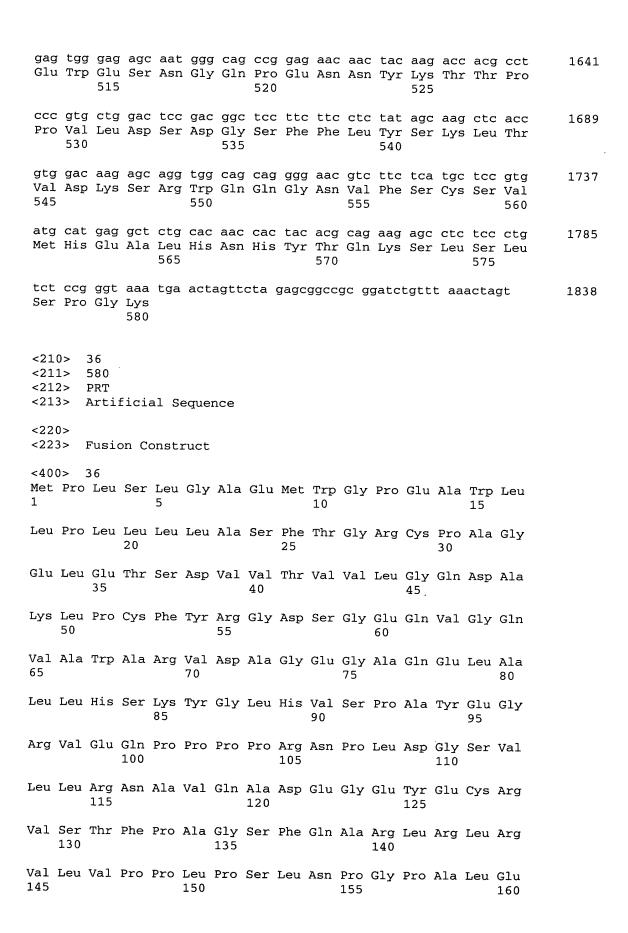
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Gln Glu Asp	Ser Gly 340	Lys Gln		Asp Le	ı Val	Ser	Ala	Ser 350	Val	Val	
Val Val Gly 355		Ala Ala	Leu 1 360	Leu Ph	e Cys	Leu	Leu 365	Va1	Val	Val	
Val Val Leu 370	Met Ser	Arg Tyr 375	His A	Arg Ar	g Lys	Ala 380	Gln	Gln	Met	Thr	
Gln Lys Tyr 385	Glu Glu	Glu Leu 390	Thr I	Leu Th	r Arg 395	Glu	Asn	Ser	Ile	Arg 400	
Arg Leu His	Ser His 405	His Thr	Asp I	Pro Arg		Gln	Pro	Glu	Glu 415	Ser	
Val Gly Leu	Arg Ala 420	Glu Gly		Pro As _l 425) Ser	Leu	Lys	Asp 430	Asn	Ser	
Ser Cys Ser 435	Val Met	Ser Glu	Glu I 440	Pro Gli	ı Gly	Arg	Ser 445	Tyr	Ser	Thr	
Leu Thr Thr 450	Val Arg	Glu Ile 455	Glu 7	Thr Gli	n Thr	Glu 460	Leu	Leu	Ser	Pro	
Gly Ser Gly 465	Arg Ala	Glu Glu 470	Glu (Glu Ası	Gln 475	Asp	Glu	Gly	Ile	Lys 480	
Gln Ala Met	Asn His 485	Phe Val	Gln (Glu Ası 490		Thr	Leu	Arg	Ala 495	Lys	
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Met Pro Leu											

ctg ccg ctg cta ctg ctg gca tca ttt aca ggc cgg tgc ccc gcg ggt

Leu Pro Leu Leu Leu Ala Ser Phe Thr Gly Arg Cys Pro Ala Gly







Glu Gly Gln Gly Leu Thr Leu Ala Ala Ser Cys Thr Ala Glu Gly Ser 165 170 175

Pro Ala Pro Ser Val Thr Trp Asp Thr Glu Val Lys Gly Thr Thr Ser 180 185 190

Ser Arg Ser Phe Lys His Ser Arg Ser Ala Ala Val Thr Ser Glu Phe 195 200 205

His Leu Val Pro Ser Arg Ser Met Asn Gly Gln Pro Leu Thr Cys Val 210 215 220

Val Ser His Pro Gly Leu Leu Gln Asp Gln Arg Ile Thr His Ile Leu 225 230 235 240

His Val Ser Phe Leu Ala Glu Ala Ser Val Arg Gly Leu Glu Asp Gln 245 250 255

Asn Leu Trp His Ile Gly Arg Glu Gly Ala Met Leu Lys Cys Leu Ser 260 265 270

Glu Gly Gln Pro Pro Pro Ser Tyr Asn Trp Thr Arg Leu Asp Gly Pro 275 280 285

Leu Pro Ser Gly Val Arg Val Asp Gly Asp Thr Leu Gly Phe Pro Pro 290 295 300

Leu Thr Thr Glu His Ser Gly Ile Tyr Val Cys His Val Ser Asn Glu 305 310 315 320

Phe Ser Ser Arg Asp Ser Gln Val Thr Val Asp Val Leu Ala Asp Pro 325 330 335

Gln Glu Asp Ser Gly Lys Gln Val Asp Leu Val Ser Ala Ser Arg Ser 340 345 350

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Glu 355 360 365

Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu 370 375 380

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser 390 395 400

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu 405 410 415

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr 420 425 430

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn 435 440 445

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro 450 455 460

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln 465 470 475 480

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val 485 490 495

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val 500 505 510

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
515 520 525

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr 530 535 540

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Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu 565 570 575

Ser Pro Gly Lys 580

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<211> 497

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<213> homo sapiens

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Leu Gly Ala Glu Met Trp Gly Pro Glu Ala Trp Leu Leu Leu Leu 20 25 30

Leu Leu Ala Ser Phe Thr Gly Arg Cys Pro Ala Gly Glu Leu Glu Thr 35 40 45

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Phe Tyr Arg Gly Asp Ser Gly Glu Gln Val Gly Gln Val Ala Trp Ala 65 70 75 80

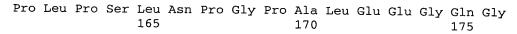
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Lys Tyr Gly Leu His Val Ser Pro Ala Tyr Glu Gly Arg Val Glu Gln
100 105 110

Pro Pro Pro Arg Asn Pro Leu Asp Gly Ser Val Leu Leu Arg Asn 115 120 125

Ala Val Gln Ala Asp Glu Gly Glu Tyr Glu Cys Arg Val Ser Thr Phe 130 135 140

Pro Ala Gly Ser Phe Gln Ala Arg Leu Arg Leu Arg Val Leu Val Pro 145 150 155 160



Leu Thr Leu Ala Ala Ser Cys Thr Ala Glu Gly Ser Pro Ala Pro Ser 180 185 190

Val Thr Trp Asp Thr Glu Val Lys Gly Thr Thr Ser Ser Arg Ser Phe 195 200 205

Lys His Ser Arg Ser Ala Ala Val Thr Ser Glu Phe His Leu Val Pro 210 215 220

Ser Arg Ser Met Asn Gly Gln Pro Leu Thr Cys Val Val Ser His Pro 225 230 235 240

Gly Leu Leu Gln Asp Gln Arg Ile Thr His Ile Leu His Val Ser Phe
245 250 255

Leu Ala Glu Ala Ser Val Arg Gly Leu Glu Asp Gln Asn Leu Trp His 260 265 270

Ile Gly Arg Glu Gly Ala Met Leu Lys Cys Leu Ser Glu Gly Gln Pro 275 280 285

Pro Pro Ser Tyr Asn Trp Thr Arg Leu Asp Gly Pro Leu Pro Ser Gly 290 295 300

Val Arg Val Asp Gly Asp Thr Leu Gly Phe Pro Pro Leu Thr Thr Glu 305 310 315 320

His Ser Gly Ile Tyr Val Cys His Val Ser Asn Glu Phe Ser Ser Arg 325 330 335

Asp Ser Gln Val Thr Val Asp Val Leu Asp Pro Gln Glu Asp Ser Gly 340 345 350

Lys Gln Val Asp Leu Val Ser Ala Ser Val Val Val Val Gly Val Ile 355 360 365

Ala Ala Leu Leu Phe Cys Leu Leu Val Val Val Val Leu Met Ser 370 375 380

Arg Tyr His Arg Arg Lys Ala Gln Gln Met Thr Gln Lys Tyr Glu Glu 385 390 395 400

Glu Leu Thr Leu Thr Arg Glu Asn Ser Ile Arg Arg Leu His Ser His 405 410 415

His Thr Asp Pro Arg Ser Gln Ser Glu Glu Pro Glu Gly Arg Ser Tyr
420 425 430

Ser Thr Leu Thr Thr Val Arg Glu Ile Glu Thr Gln Thr Glu Leu Leu 435 440 445

Ser Pro Gly Ser Gly Arg Ala Glu Glu Glu Glu Asp Gln Asp Glu Gly 450 455 460

Ile Lys Gln Ala Met Asn His Phe Val Gln Glu Asn Gly Thr Leu Arg
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Ala Lys Pro Thr Gly Asn Gly Ile Tyr Ile Asn Gly Arg Gly His Leu
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Val

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Leu Leu Ala Ser Phe Thr Val Pro Pro Leu Pro Ser Leu Asn Pro Gly 35 40 45

Pro Ala Leu Glu Glu Gly Gln Gly Leu Thr Leu Ala Ala Ser Cys Thr 50 55 60

Ala Glu Gly Ser Pro Ala Pro Ser Val Thr Trp Asp Thr Glu Val Lys 70 75 80

Gly Thr Thr Ser Ser Arg Ser Phe Lys His Ser Arg Ser Ala Ala Val85 90 95

Thr Ser Glu Phe His Leu Val Pro Ser Arg Ser Met Asn Gly Gln Pro 100 105 110

Leu Thr Cys Val Val Ser His Pro Gly Leu Leu Gln Asp Gln Arg Ile 115 120 125

Thr His Ile Leu His Val Ser Phe Leu Ala Glu Ala Ser Val Arg Gly 130 135 140

Leu Glu Asp Gln Asn Leu Trp His Ile Gly Arg Glu Gly Ala Met Leu 145 150 155 160

Lys Cys Leu Ser Glu Gly Gln Pro Pro Pro Ser Tyr Asn Trp Thr Arg 165 170 175

Leu Asp Gly Pro Leu Pro Ser Gly Val Arg Val Asp Gly Asp Thr Leu 180 185 190

Gly Phe Pro Pro Leu Thr Thr Glu His Ser Gly Ile Tyr Val Cys His 195 200 205

Val Ser Asn Glu Phe Ser Ser Arg Asp Ser Gln Val Thr Val Asp Val 210 215 220

Leu Asp Pro Gln Glu Asp Ser Gly Lys Gln Val Asp Leu Val Ser Ala 225 230 235 240 Ser Val Val Val Gly Val Ile Ala Ala Leu Leu Phe Cys Leu Leu 245 250 255

Val Val Val Val Leu Met Ser Arg Tyr His Arg Arg Lys Ala Gln 260 265 270

Gln Met Thr Gln Lys Tyr Glu Glu Glu Leu Thr Leu Thr Arg Glu Asn 275 280 285

Ser Ile Arg Arg Leu His Ser His His Thr Asp Pro Arg Ser Gln Pro 290 295 300

Glu Glu Ser Val Gly Leu Arg Ala Glu Gly His Pro Asp Ser Leu Lys 305 310 315 320

Asp Asn Ser Ser Cys Ser Val Met Ser Glu Glu Pro Glu Gly Arg Ser 325 330 335

Tyr Ser Thr Leu Thr Thr Val Arg Glu Ile Glu Thr Gln Thr Glu Leu 340 345 350

Leu Ser Pro Gly Ser Gly Arg Ala Glu Glu Glu Glu Asp Gln Asp Glu 355 360 365

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Leu Val

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<213> homo sapiens

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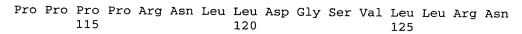
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Arg Val Asp Ala Gly Glu Gly Ala Gln Glu Leu Ala Leu Leu His Ser 85 90 95

Lys Tyr Gly Leu His Val Ser Pro Ala Tyr Glu Gly Arg Val Glu Gln 100 105 110



Ala Val Gln Ala Asp Glu Gly Glu Tyr Glu Cys Arg Val Ser Thr Phe 130 135 140

Pro Ala Gly Ser Phe Gln Ala Arg Leu Arg Leu Arg Val Leu Val Pro 145 150 155 160

Pro Leu Pro Ser Leu Asn Pro Gly Pro Ala Leu Glu Glu Gly Gln Gly 165 170 175

Leu Thr Leu Ala Ala Ser Cys Thr Ala Glu Gly Ser Pro Ala Pro Ser 180 185 190

Val Thr Trp Asp Thr Glu Val Lys Gly Thr Thr Ser Ser Arg Ser Phe 195 200 205

Lys His Ser Arg Ser Ala Ala Val Thr Ser Glu Phe His Leu Val Pro 210 215 220

Ser Arg Ser Met Asn Gly Gln Pro Leu Thr Cys Val Val Ser His Pro 225 230 235 240

Gly Leu Leu Gln Asp Gln Arg Ile Thr His Ile Leu His Val Ser Phe 245 250 255

Leu Ala Glu Ala Ser Val Arg Gly Leu Glu Asp Gln Asn Leu Trp His 260 265 270

Ile Gly Arg Glu Gly Ala Met Leu Lys Cys Leu Ser Glu Gly Gln Pro 275 280 285

Pro Pro Ser Tyr Asn Trp Thr Arg Leu Asp Gly Pro Leu Pro Ser Gly 290 295 300

Val Arg Val Asp Gly Asp Thr Leu Gly Phe Pro Pro Leu Thr Thr Glu 305 310 315 320

His Ser Gly Ile Tyr Val Cys His Val Ser Asn Glu Phe Ser Ser Arg 325 330 335

Asp Ser Gln Val Thr Val Asp Val Leu Ala Asp Pro Gln Glu Asp Ser 340 345 350

Gly Lys Gln Val Asp Leu Val Ser Ala Ser Val Val Val Gly Val 355 360 365

Ile Ala Ala Leu Leu Phe Cys Leu Leu Val Val Val Val Leu Met 370 375 380

Ser Arg Tyr His Arg Arg Lys Ala Gln Gln Met Thr Gln Lys Tyr Glu 385 390 395 400

Glu Glu Leu Thr Leu Thr Arg Glu Asn Ser Ile Arg Arg Leu His Ser 405 410 415

His His Thr Asp Pro Arg Ser Gln Ser Glu Glu Pro Glu Gly Arg Ser 420 425 430

Tyr Ser Thr Leu Thr Thr Val Arg Glu Ile Glu Thr Gln Ala Glu Leu 435 440 445

Leu Ser Pro Gly Ser Gly Arg Ala Glu Glu Glu Glu Asp Gln Asp Glu 450 455 460

Gly Ile Lys Gln Ala Met Asn His Phe Val Gln Glu Asn Gly Thr Leu 465 470 475 480

Arg Ala Lys Pro Thr Gly Asn Gly Ile Tyr Ile Asn Gly Arg Gly His 485 490 495

Leu Val